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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,568	09/15/2003	Steven Z. Wu	50623.335	2840

7590 05/24/2010

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EXAMINER	
SHEIKH, HUMERA N	
ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
05/24/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/663,568	WU ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,28-32 and 34-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,28-32 and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response after Final Office Action and Applicant's Arguments/Remarks, filed 07/21/09 and the Appeal Brief filed 02/17/10 is acknowledged.

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

In view of the Appeal Brief, PROSECUTION IS HEREBY REOPENED.

Please Note: Previously withdrawn (non-elected) claims 36-37 have now been rejoined and examined with the elected invention.

The following are the new grounds of rejection:

Claims 25, 28-32 and 34-37 are pending in this action. Claims 1-24, 26, 27 and 33 have been cancelled. Claims 25, 28-32 and 34-37 are rejected.

* * * * *

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a coating layer that is 'not' free from therapeutic substances, does not reasonably provide enablement for "a coating layer that is free from any therapeutic substances" as currently claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or

use the invention commensurate in scope with these claims. Applicant has not shown how to make and obtain a drug-free coating, particularly in view of the fact that the coating layer comprises "polymeric particles containing a therapeutic substance". Therefore, it cannot be seen as to how the coating layer would be "free from any therapeutic substances" since Applicants are claiming *polymeric particles containing a therapeutic substance*, which are embedded within the coating layer. Hence, the claims contain contradicting language in that they require drug and yet simultaneously desire to avoid drug in the coating layer.

* * * * *

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25 and 32 recite "polymeric particles containing a therapeutic substance, which are embedded within the coating layer, wherein the coating layer is free from any therapeutic substances". The claim language is indefinite because it is confusing and unclear as to how the coating layer can "be free from any therapeutic substances" when the claim explicitly recites "polymeric particles containing a therapeutic substance". The language in the claims is contradictory claim language in that they require drug and yet simultaneously desire to avoid drug in the coating layer. How can there be a drug-free coating layer when the coating layer specifically requires drug/polymer particles in it? Clarification is requested.

* * * * *

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 32, 34, 36 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Ding *et al.* (hereinafter "Ding") (U.S. Pat. No. 6,099,562).

Ding ('562) discloses a medical device, coating and method for coating an implantable stent wherein a relatively thin layer of biostable elastomeric material in which biologically active material is dispersed as a coating is applied on the surfaces of the stent prosthesis (col. 3, line 60 – col. 4, line 7). The coating is preferably applied as a mixture, solution or suspension of polymeric material and finely divided biologically active species dispersed in an organic vehicle or a solution or partial solution of such species in a solvent or vehicle for the polymer and/or biologically active species (col. 4, lines 8-13). This reads on Applicant's medical device having a 'coating layer wherein the therapeutic substance completely encased within the polymer particles' and a 'film layer including polymeric material encasing the polymeric particles'. The term "finely divided" refers to any type or size of included material from dissolved molecules through suspensions, colloids and particulate mixtures. The active material is dispersed in a carrier material which may be the polymer, a solvent or both. The coating is preferably applied as a plurality of relatively thin layers sequentially applied in relatively rapid sequence and is preferably applied with the stent in a radially expanded state (col. 4, lines 14-21). Ding discloses

that the coating may be applied by dipping or spraying using evaporative solvent materials of relatively high vapor pressure (col. 4, line 66 – col. 5, line 9).

The layered coating is referred to as the undercoat and topcoat. Typically most or all of the biologically active material is contained in the undercoat and a non-thrombogenic or biocompatible non-porous surface found in the topcoat (col. 4, lines 22-30); (col. 6, lines 6-14). The topcoat can cover either the entire undercoat or only part of the undercoat before or after implantation (col. 6, lines 50-54). In this regard, Fig. 8 demonstrates use of a topcoat containing Fluorosilicone (FSi) *only* (i.e., no drug) as compared with a Fsi topcoat containing heparin (col. 8, lines 54-57). Thus, based upon this reading the topcoat layer is free from therapeutic substance(s). In addition, column 15, lines 25-30 indicates that the layers can be used which have *no drug loadings* at all. For example, a pulsatile heparin release system may be achieved by a coating in which alternate layers containing heparin are sandwiched between unloaded layers of silicone or other materials for a portion of the coating. Thus, various combinations can be obtained with respect to controlling the release of biologically active materials. Suitable active materials disclosed include agents that inhibit hyperplasia and particularly, restenosis (col. 7, lines 30-53).

Hence, Ding discloses a medical device (i.e., stent) and coating method comprising application of a suspension, colloids and particulate mixtures whereby polymer/drug has been dispersed in an organic phase or vehicle/carrier. Ding discloses that such a process enables an effective method of coating an implant, such as a stent whereby a relatively thin layer of or multi-layer coating of biostable elastomeric material in which active material is dispersed can be achieved. The device comprises both an undercoat and topcoat, whereby the topcoat can be free

of drug or therapeutic substances. The coating is applied onto the surfaces of the stent such as by spraying and the amount of active substance can be varied using this process.

These teachings read on the limitations of instant claims 32, 34, 36 and 37.

Thus, Ding anticipates the present claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 25, 28-31 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ding *et al.* (hereinafter "Ding") (U.S. Pat. No. 6,099,562) in view of Lentz *et al.* (hereinafter "Lentz") (US Pat. Appln. Pub. No. 2002/0133183) and further in view of Hunter *et al.* (hereinafter "Hunter") (U.S. Patent No. 5,886,026).

Ding ('562), as discussed above, teaches a medical device, coating and method for coating an implantable stent wherein a relatively thin layer of biostable elastomeric material in

which biologically active material is dispersed as a coating is applied on the surfaces of the stent prosthesis (col. 3, line 60 – col. 4, line 7). The coating is preferably applied as a mixture, solution or suspension of polymeric material and finely divided biologically active species dispersed in an organic vehicle or a solution or partial solution of such species in a solvent or vehicle for the polymer and/or biologically active species (col. 4, lines 8-13). This reads on Applicant's medical device having a 'coating layer wherein the therapeutic substance completely encased within the polymer particles' and a 'film layer including polymeric material encasing the polymeric particles'. The term "finely divided" refers to any type or size of included material from dissolved molecules through suspensions, colloids and particulate mixtures. The active material is dispersed in a carrier material which may be the polymer, a solvent or both. The coating is preferably applied as a plurality of relatively thin layers sequentially applied in relatively rapid sequence and is preferably applied with the stent in a radially expanded state (col. 4, lines 14-21). Ding discloses that the coating may be applied by dipping or spraying using evaporative solvent materials of relatively high vapor pressure (col. 4, line 66 – col. 5, line 9).

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have *no drug loadings* at all. For example, a pulsatile heparin release system may be achieved by a coating in which alternate layers containing heparin are sandwiched between unloaded layers of silicone or other materials for a portion of the coating. Thus, various combinations can be obtained with respect to controlling the release of biologically active materials. Suitable active materials disclosed include agents that inhibit hyperplasia and particularly, restenosis (col. 7, lines 30-53).

Hence, Ding discloses a medical device (i.e., stent) and coating method comprising application of a suspension, colloids and particulate mixtures whereby polymer/drug has been dispersed in an organic phase or vehicle/carrier. Ding discloses that such a process enables an effective method of coating an implant, such as a stent whereby a relatively thin layer of or multi-layer coating of biostable elastomeric material in which active material is dispersed can be achieved. The device comprises both an undercoat and topcoat, whereby the topcoat can be free of drug or therapeutic substances. The coating is applied onto the surfaces of the stent such as by spraying and the amount of active substance can be varied using this process.

Ding does not teach that their "coating layer comprises a polymer different from the polymer from which the particles are made".

Lentz ('183) teaches implantable medical devices, such as stents, provided with polymeric coatings (i.e., polyfluoro copolymers) and films to deliver pharmaceutically active material (page 8, ¶ 0084, Abstract), whereby particles of drug are fully encapsulated in the polymer (page 9, ¶ 0088) and wherein different polyfluoro copolymers may be used for different layers in the stent coating. The individual coatings may be prepared from different polyfluoro

copolymers (page 8, ¶ 0084). Blends of polyfluoro copolymers may also be used. The use of different polymeric coatings provides a desired balance of coating properties, i.e., elasticity, toughness, etc. and drug delivery characteristics, such as release profile (page 8-9, ¶s 0086-0087). Lentz teaches that in cases where a dispersion is applied to the stent and the smoothness of the coating film surface requires improvement, or to be ensured that all particles of the drug are fully encapsulated in the polymer or in cases where the release rate of the drug is to be slowed, a clear topcoat used to provide sustained release of the drug or another polyfluoro copolymer that further restricts the diffusion of the drug out of the coating may be applied (page 9, ¶ 0088).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate different polymeric coatings onto an implantable medical device, such as a stent, as taught by Lentz, within the devices of Ding. One would do so with a reasonable expectation of success because Lentz explicitly teaches implantable medical devices (i.e., stents) provided with polymeric coatings (i.e., polyfluoro copolymers) to deliver pharmaceutically active material, whereby particles of drug are fully encapsulated in the polymer and wherein different polyfluoro copolymers may be used for different layers in the stent coating. The use of different polymeric coatings provides a desired balance of coating properties, i.e., elasticity, toughness, etc. and drug delivery characteristics, such as release profile. The expected result would be an improved drug-loaded stent for the delivery of various active agents.

The teachings of Ding are discussed above. Ding does not teach particles of 0.5 to 2 microns in size (instant claim 29). It is the position of the Examiner that the determination of

suitable or effective particle sizes can be carried out via routine or manipulative experimentation by the skilled artisan to obtain optimal results, as these are variable parameters attainable within the art. Nonetheless, the Hunter reference ('026) teaches particle sizes as presently claimed.

Hunter ('026) teaches compositions comprising anti-angiogenic factors and polymeric carriers, stents which have been coated with such compositions and methods for utilizing the stents and compositions (see column 1, lines 15-20); (col. 4, lines 25-45); (col. 37, line 31 – col. 38, line 4) and claims. The stents may be self-expanding, balloon expandable or implanted by a change in temperature (col. 23, lines 23-42). In preferred embodiments, the anti-angiogenic compositions are provided in non-capsular formulations such as microspheres (ranging from nanometers to micrometers in size), as well as pastes, films and sprays (col. 16, line 63 - col. 17, line 11). The sprays may be prepared from microspheres having a size of for example, from 0.1 μm to 3μm (this range falls within and meets Applicant's claimed range of 0.5 to 2 microns in size of instant claim 29) (col. 17, lines 30-65).

Hunter teaches that the stents may be coated with the anti-angiogenic compositions in various manners, including for example: (a) by directly affixing to the stent an anti-angiogenic composition (e.g., by either spraying the stent with a polymer/drug film or by dipping the stent into a polymer/drug solution); (b) by coating the stent with a substance such as a hydrogel which will in turn absorb the anti-angiogenic composition; (c) by interweaving anti-angiogenic factor coated thread (or the polymer itself formed into a thread) into the stent structure; (d) by inserting the stent into a sleeve or mesh which is comprised of or coated with an anti-angiogenic composition; or (e) constructing the stent itself with an anti-angiogenic composition (col. 22, line 8 – col. 23, line 10). Hunter teaches that for vascular stents, the composition should not render

the stent thrombogenic (causing blood clots to form) or cause significant turbulence in blood flow (more than the stent itself would be expected to cause if it was uncoated) (see col. 23, lines 2-10).

The anti-angiogenic compositions may additionally comprise a wide variety of compounds in addition to the anti-angiogenic factor and polymeric carrier (col. 15, line 16 - col. 16, line 35). The manufacturing process of the microspheres and the manufacturing process of the stent coating is discussed at column 45, line 31 – column 48, line 59. Also see column 54, lines 24-51, whereby preparation of control microspheres (drug absent) are discussed.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide for microspheres having a size of from 0.1 μm to 3μm (this range meeting Applicant's claimed range of 0.5 to 2 microns) as taught by Hunter, within the devices of Ding. One would do so with a reasonable expectation of success because Hunter explicitly teaches implantable medical devices (i.e., stents) provided with microspheres having a size of from 0.1 μm to 3μm and suggests that these are suitable particle sizes that yield effective results. The expected result would be an improved drug-loaded stent for the delivery of active agents.

* * * * *

Pertinent Art

- Whitbourne *et al.* (US 2004/01107007) :

Whitbourne discloses a medicated, multi-layered coating stent.

* * * * *

Response to Arguments

Applicant's arguments with respect to claims 25, 28-32 and 34-35 have been considered but are moot in view of the new ground(s) of rejection.

* * * * *

Conclusion

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1615

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